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(30)Priority
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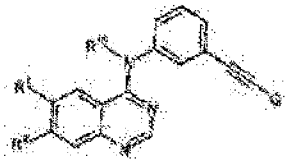
(54) METHOD AND INTERMEDIATE FOR PRODUCING ANTICANCER COMPOUND

(57)Abstract:
PROBLEM TO BE SOLVED: To obtain an anticancer compound in a high yield useful for treating a highly proliferative disorder such as cancer in mammals by using a specific synthetic intermediate.
SOLUTION: (A) A compound of formula I [R1 and R2 are each a 1-10C alkyl, a 1-10C alkoxy, preferably R1 and R2 are each 2-methoxyethoxy; R15 is H, a 1-10C alkyl or the like, preferably H; G is C(OH)R3R4 or SiR3R4R5 (R3 to R5 are each a 1-6C alkyl)] is treated, (B) in the case of G being C (OH)R3 R4, with an alkaline (earth) metal hydroxide in a hydroxy-substituted 1-10C alkyl-containing solvent or, (C) in the case of G being SiR3R4R5, with a tetra (1-6C alkyl) ammonium fluoride compound in an aprotic solvent to give a compound of formula II. The compound of formula I can be obtained by treating a compound of formula III with a compound of formula IV.



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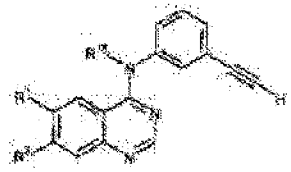

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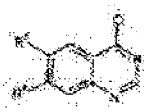

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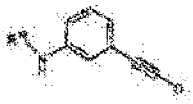

IV

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前置審査

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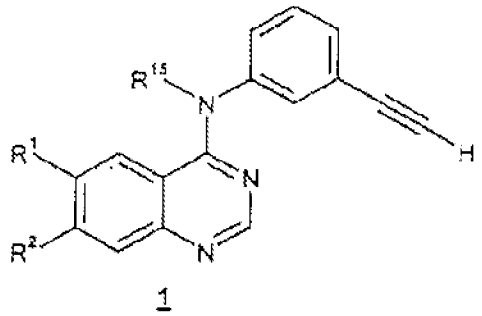
(54)【発明の名称】　抗癌性化合物を製造するための方法と中間体

1



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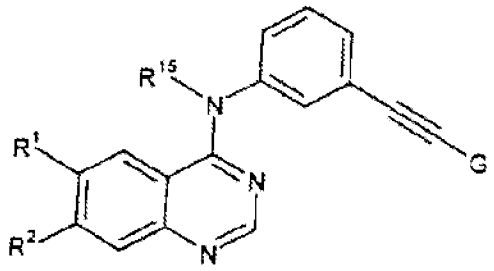

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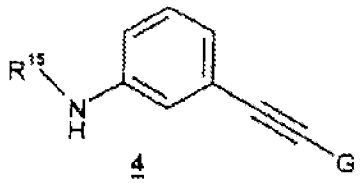

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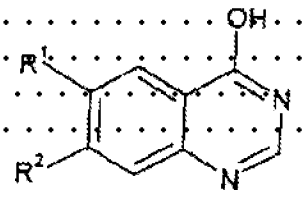

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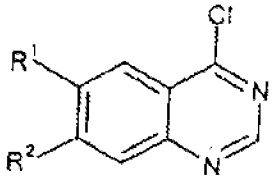

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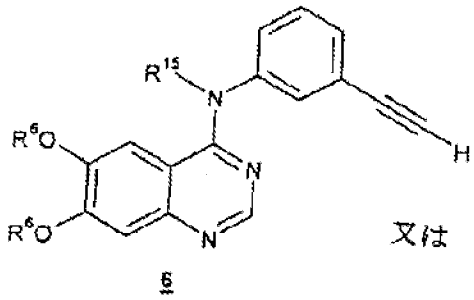

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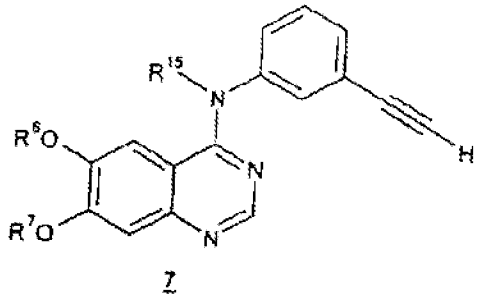

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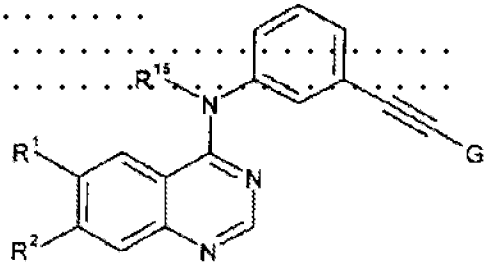

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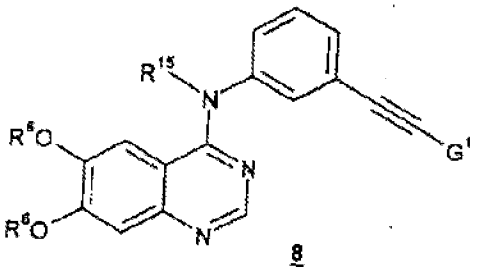

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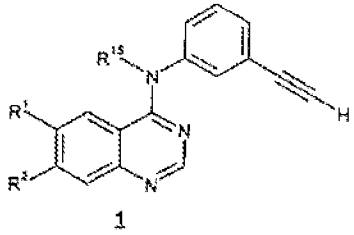

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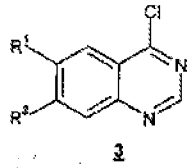

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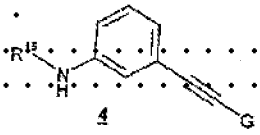

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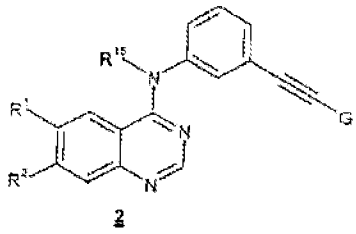

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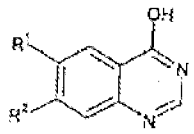

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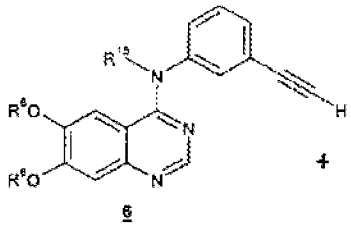

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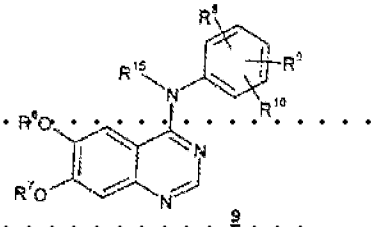

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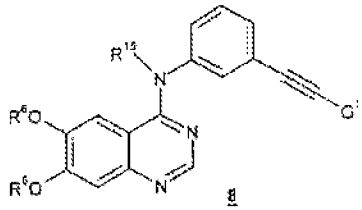

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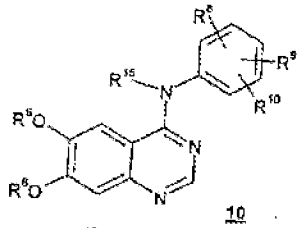

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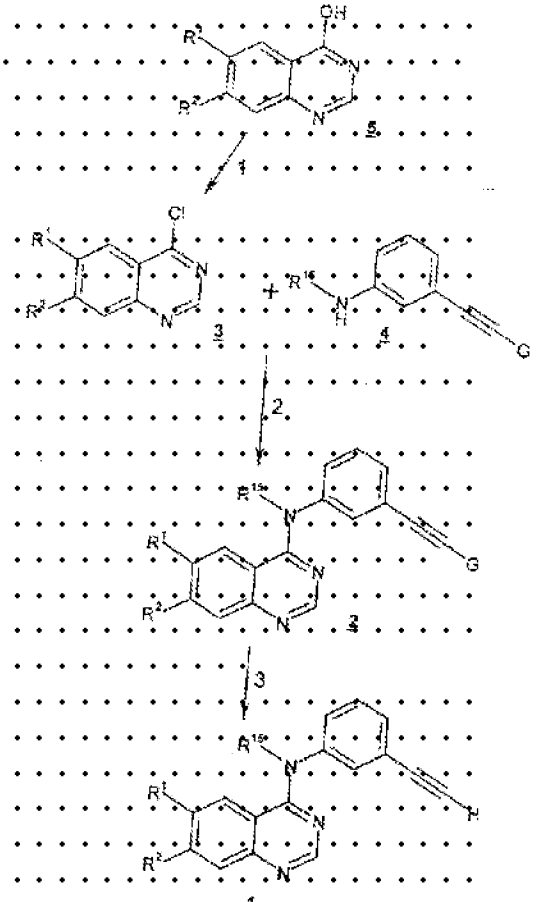

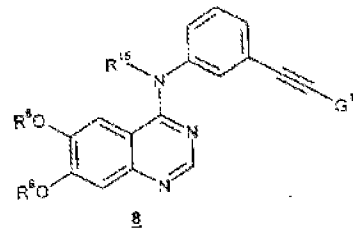

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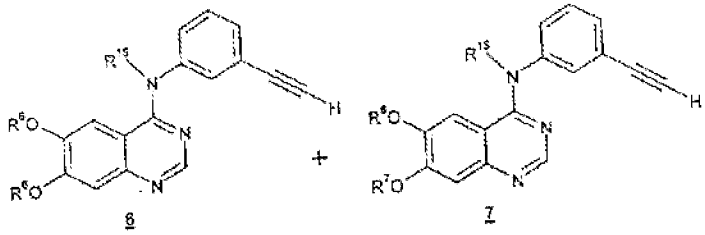

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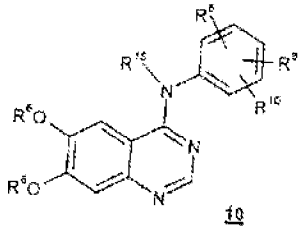

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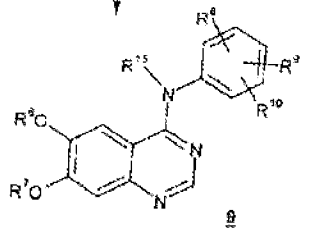

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δ_H (300 MHz, $CDCl_3$) 0.24 (9H, s), 3.56 (2H, bs), 6.62 (1H, ddd, J = 1.0, 2.3 & 8.0), 6.76 (1H, t, J = 2.2), 6.87 (1H, dt, J = 7.7 & 1.2), 7.07 (1H, t, J = 7.8); δ_C (75.5 MHz; $CDCl_3$) 93.4, 105.4, 115.6, 118.2, 122.4, 123.8, 129.2, 146.2; m/e 190 $(M+H)^+$

δ_H (400 MHz; $CDCl_3$) 0.21 (9H, s), 3.38 (3H, s), 3.41 (3H, s), 3.72 (2H, m), 3.77 (2H, m), 4.10 (2H, s), 4.53 (2H, s), 7.20 (1H, t, J = 7.8), 7.23-7.28 (2H, m), 7.75 (1H, d, J 7.8), 7.88 (1H, s), 8.20 (1H, s), 8.42 (1H, s); m/e 466 $(M+H)^+$

δ_H (300 MHz; d_6-DMSO) 3.36 (6H, s), 3.77-3.80 (4H, m), 4.30 (1H, s), 7.39 (1H, s), 7.41 (1H, d, J = 7.8), 7.50 (1H, t, J = 7.9), 7.79 (1H, d, J = 8.1), 7.88 (1H, s), 8.40 (1H, s), 8.86 (1H, s), 11.48 (1H, bs); δ_C (100 MHz; d_6-DMSO) 58.4, 58.5, 68.7, 69.2, 69.7, 97.6, 81.3, 83.0, 100.3, 105.2, 107.2, 121.9, 125.4, 127.6, 128.9, 129.2, 135.2, 137.7, 146.3, 149.2, 155.4, 156.0; m/e 394 $(M+H)^+$

δ_H (400 MHz; d_6-DMSO) 1.44 (6H,s), 3.31-3.32 (5H, m), 3.65-3.75 (4H, m), 4.24-4.30 (2H, m), 4.35-4.37 (2H, m),7.25 (1H, m), 7.39 (2H, m), 7.72-7.74 (2H, m), 8.47 (1H, s), 8.79 (1H, s), 11.64 (1H, s); m/e 452 $(M+H)^+$

δ_H (400 MHz; $CDCl_3$): 1.56 (6H,s), 3.35 (3H,s), 3.37 (3H, s), 3.7-3.71 (4H, m), 4.13-4.19 (4H, m), 7.3 (1H, m), 7.13-7.17 (2H, m), 7.3 (1H, m), 7.6 (2H, m), 8.55 (1H, s); m/e 452 $(M+H)^+$

mp 72-74°C;

δ_H (360 MHz; $CDCl_3$) 1.16 (3H, t, J = 7.6), 2.58 (2H, q, J = 7.6), 3.32 (3H, s), 3.94 (3H, s), 2.01-2.47 (2H, m), 2.08-2.54 (2H, m), 4.07-4.12 (4H, m), 6.91 (1H, d, J = 7.6), 7.11 (1H, s), 7.21 (1H, t, J = 7.8), 7.35 (1H, s), 7.42 (1H, s), 7.48 (1H, d, J = 8.0), 8.13 (1H, bs), 8.55 (1H, s); δ_C (75.5 MHz; $CDCl_3$) 15.4, 28.8, 59.1, 68.2, 68.9, 70.4, 70.8, 103.0, 108.3, 108.3, 119.7, 121.7, 123.9, 128.8, 138.6, 145.1, 147.0, 148.5, 153.6, 154.4, 156.9; ν_{max} (KBr) cm^{-1} 3136 (s), 1624 (s), 1575 (s), 1535 (s), 1487 (s); m/z 398 $(M+H)^+$ (実測値 C, 65.64; H, 6.96; N, 10.32. $C_{22}H_{23}N_3O_4 \cdot 0.25H_2O$：計算値 C, 65.73; H, 6.90; N, 10.45%).

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δ_H (300 MHz; $CDCl_3$) 1.17 (3H, t, J 7.6), 2.55 (2H, q, J 7.6), 3.33 (3H, s), 3.55-3.66 (2H, m), 4.07-4.11 (2H, m), 5.11 (2H, s), 6.93 (1H, d, J 7.7), 7.18-7.29 (5H, m), 7.35-7.42 (4H, m), 7.50 (1H, d, J 8.0), 8.20 (1H, bs), 8.51 (1H, s); δ_C (75.5 MHz; $CDCl_3$) 14.2, 15.4, 28.6, 59.2, 69.2, 70.7, 70.8, 103.2, 105.1, 109.4, 119.7, 121.7, 124.0, 127.3, 128.1, 128.5, 128.8, 135.8, 138.6, 145.1, 147.0, 148.5, 153.7, 154.2, 156.9; ν_{max} (KBr) cm^{-1} 1625, 1611, 1576; m/z 430 $(M+H)^+$; (実測値 C, 71.42; H, 6.50; N, 9.46. $C_{26}H_{27}N_3O_3$ · 計算値 C, 72.70; H, 6.34; N, 9.78%).

δ_H (300 MHz; $CDCl_3$) 0.93 (3H, t, J 7.4), 1.19 (3H, t, J 7.6), 1.45 (2H, 六重線, J 7.5), 1.79 (2H, 五重線, J 6.9), 2.61 (2H, q, J 7.6), 3.38 (3H, s), 3.70-3.74 (2H, m), 4.00 (2H, t, J 6.6), 4.12-4.15 (2H, m), 6.94 (1H, d, J 7.7), 7.16 (1H, s), 7.24 (1H, t, J 7.6), 7.34 (1H, s), 7.44 (1H, s), 7.51 (1H, d, J 8.0), 7.95 (1H, bs), 8.60 (1H, s); δ_C (75.5 MHz; $CDCl_3$) 13.8, 15.4, 19.2, 28.6, 30.8, 59.3, 68.7, 69.3, 70.9, 103.2, 103.2, 106.9, 119.6, 121.6, 124.0, 128.9, 138.6, 145.2, 147.2, 148.8, 153.6, 154.9, 156.8; ν_{max} (KBr) cm^{-1} 1618, 1576, 1519; m/z 396 $(M+H)^+$; (実測値 C, 70.90; H, 7.56; N, 10.66. $C_{23}H_{25}N_3O_3$ · 計算値: C, 69.85; H, 7.39; N, 10.63%).

δ_H (300 MHz; $CDCl_3$) 3.31 (3H, s), 3.35 (3H, s), 3.62-3.65 (2H, m), 3.70-3.72 (2H, m), 3.74 (3H, s), 4.04-4.11 (4H, m), 6.83 (2H, d, J 9.0), 7.09 (1H, s), 7.33 (1H, s), 7.46 (2H, d, J 9.0), 8.12 (1H, bs), 1H, s); δ_C (75.5 MHz; $CDCl_3$) 55.4, 59.2, 68.2, 69.9, 70.4, 70.8, 103.1, 106.3, 109.1, 114.2, 124.7, 131.4, 146.8, 148.5, 153.7, 154.3, 156.7, 157.3; ν_{max} (KBr) cm^{-1} 1619, 1590, 1562, 1511; m/z 400 $(M+H)^+$. (実測値 C, 63.30; H, 6.37; N, 10.47. $C_{21}H_{25}N_3O_5$ 計算値 C, 63.42; H, 6.31; N, 10.52%)

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δ_H (300 MHz; $CDCl_3$) 3.34 (3H, s), 3.91 (2H, t, J 4.2), 3.74 (3H, s), 4.10 (2H, bs), 5.13 (2H, s), 5.83 (2H, d, J 8.9), 7.20-7.30 (5H, m), 7.36-7.38 (3H, m), 7.47 (2H, d, J 8.9), 8.10 (1H, bs), 8.54 (1H, s); δ_C (75.5 MHz, $CDCl_3$) 55.5, 59.3, 69.2, 70.7, 70.9, 103.3, 109.0, 109.1, 114.2, 124.6, 127.3, 128.1, 128.5, 131.3, 135.8, 146.8, 148.5, 153.7, 154.2, 154.2, 156.8, 157.2; ν_{max} (KBr) cm^{-1} 1619, 1580, 1511; m/z 432 $(M+H)^+$; (実測値 C, 69.46; H, 5.85; N, 9.68. $C_{25}H_{25}N_3O_4$ 計算値: C, 69.59; H, 5.84; N, 9.74%).

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δ_H (300 MHz, $CDCl_3$) 3.33 (3H, s), 3.39 (3H, s), 3.42-3.45 (2H, m), 3.48-3.51 (2H, m), 3.58 (3H, s), 3.74-3.78 (2H, m), 4.16-4.20 (2H, m), 6.33 (1H, s), 7.11-7.20 (4H, m), 7.63 (2H, t, J 7.8), 8.66 (1H, s); δ_C (75.5 MHz: $CDCl_3$) 42.0, 59.2, 59.3, 67.6, 68.2, 70.3, 70.4, 106.5, 107.9, 110.9, 125.8, 126.0, 126.9, 147.0, 148.4, 148.7, 153.0, 153.4, 160.4, ν_{max} (KBr) cm^{-1} 1615, 1571, 1497; m/z 384 $(M+H)^+$; (実測値 C, 55.65; H, 5.52; N, 11.01. $C_{21}H_{25}N_3O_6$ 計算値 C, 65.78; H, 6.57; N, 10.96%).

δ_H (300 MHz; $CDCl_3$) 0.93 (3H, t, J 7.4), 1.45 (2H, 六重線 J 7.4), 1.80 (2H, 五重線, J 6.7), 3.35 (3H, s), 3.44-3.52 (4H, m), 3.59 (3H, s), 4.05 (2H, t, J 6.7), 6.34 (1H, s), 7.12-7.21 (4H, m), 7.34 (2H, t, J 7.7), 8.69 (1H, s); δ_C (75.5 MHz; $CDCl_3$) 13.8, 19.2, 30.7, 42.0, 59.2, 67.8, 68.6, 70.4, 106.5, 107.7, 110.8, 125.8, 125.9, 129.9, 147.0, 148.6, 153.0, 153.8, 160.4; ν_{max} (KBr) cm^{-1} 1616, 1572, 1545; m/z 382 $(M+H)^+$; (実測値 C, 69.39; H, 7.38; N, 10.86. $C_{22}H_{27}N_3O_5$ 計算値: C, 69.27; H, 7.14; N, 11.02%).